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CHEMISTRY OF NEOPENTYL DERIVATIVES

I. AMBIDENCY OF THE BENZYL GRIGNARD REAGENT IN REACTION WITH t-BUTYL HALIDES. SYNTHESIS AND THERMODYNAMIC DISSOCIATION CONSTANTS OF NEOPENTYLBENZOIC ACIDS

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Abstract—The reaction of benzylmagnesium halides with t-butyl halides yields *o*- and *p*-t-butyltoluene in addition to neopentylbenzene. A study has been made of the influence of (i) the halide atoms present in both reactants, (ii) the purity of the magnesium used, (iii) the solvent in which the reaction is conducted, and (iv) the substituents in the aromatic ring of the benzyl Grignard reagent. The reaction of t-butylmagnesium chloride with 4-alkylbenzyl chlorides has also been investigated.

The neopentyltoluenes can be oxidized selectively to the corresponding neopentylbenzoic acids. The pK_a^*-values of these acids have been determined in 50 vol % EtOH and are compared with those of sixteen other monoalkyl-substituted benzoic acids.

INTRODUCTION

The ambidency of the benzyl Grignard reagent, i.e. the tendency to give *ortho* and *para* substituted toluenes in addition to the "normal" product, has been known for a long time.[1] Recent work of Benkeser *et al.* and of other authors[2] has given rise to a renewed interest in this phenomenon. Up till now, however, no mention has been made of the ambidency of benzylmagnesium halides in reaction with alkyl halides. In order to investigate the possibility of "abnormal" products being formed in this type of reaction, we have reacted t-butyl halides with benzylmagnesium halides. This reaction has frequently been used for the preparation of neopentyl-substituted aromatic compounds, particularly neopentylbenzene.[3] We have tried to establish the influence on the reaction course of (i) the halide atoms present in both reactants, (ii) the purity of the magnesium used in the preparation of the Grignard reagent, (iii) the solvent in which the reaction was conducted, and (iv) the substituents in the aromatic ring of the benzylmagnesium halide. We have also studied the inverse of this Grignard reaction, i.e. that of t-butylmagnesium chloride with 4-alkylbenzyl chlorides.

The neopentyltoluenes obtained in the course of this investigation were oxidized in high yields to the corresponding neopentylbenzoic acids by means of alkaline potassium permanganate in aqueous pyridine. The thermodynamic dissociation constants of the acids were determined and compared with the pK_a^*-values of other monoalkyl-substituted benzoic acids obtained in this laboratory.

RESULTS AND DISCUSSION

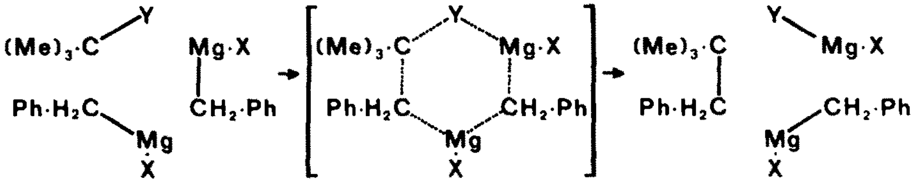
A. *The Grignard reaction*

The reaction of benzylmagnesium halides with t-butyl halides has been studied by us in detail. First we have tested the variation of the halide atoms in both reactants and the influence of the purity of the magnesium used in the preparation of the Grignard reagent. Ether was used as the solvent and a molar ratio of 1:1 was chosen.

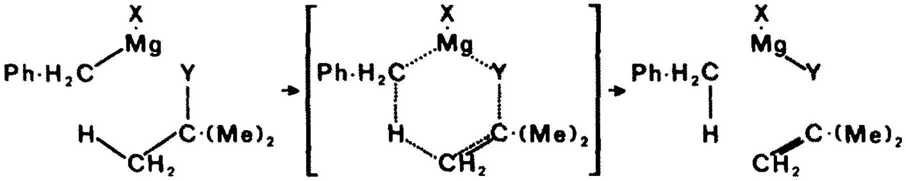
The reactions of benzylmagnesium chloride and bromide with t-butyl chloride and bromide in ether give an average yield of 40% of the normal product neopentylbenzene along with varying amounts of *o*-t-butyltoluene (0·6–3·8%) and *p*-t-butyltoluene (0·6–2·6%). There appears to be little influence on the product distribution by the halide atoms or by the purity of the magnesium used.

Berliner and Berliner[4] found that if the reaction was conducted in an ether : benzene mixture the neopentylbenzene was contaminated with *p*-t-butyltoluene. We found that in addition to *p*- also some *o*-t-butyltoluene was formed. Other reaction products were isobutene, toluene, bibenzyl, and *trans*-stilbene.

Two groups of products formed in the reaction can be distinguished: As normal products we regard neopentylbenzene, isobutene, toluene, bibenzyl, and *trans*-stilbene. The formation of all these products can be readily understood. It has been suggested that condensation products like neopentylbenzene are the result of a reaction between two molecules of Grignard reagent and one of alkyl halide. This can be formulated in terms of a quasi 6-membered transition state:[5]

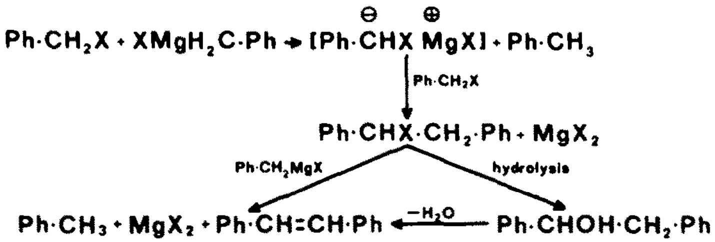


As for the formation of isobutene and toluene another quasi 6-membered ring transition state can be assumed:



Toluene does not originate from the hydrolysis of unreacted Grignard reagent, because before the addition of water solid carbon dioxide was added to the reaction mixture. After hydrolysis only traces of phenylacetic acid could be detected, showing that almost all of the Grignard reagent had reacted with the t-butyl halide.

The origin of *trans*-stilbene can be explained in analogy to its formation from benzyllithium:[6]



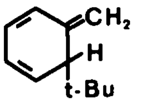
Thus *trans*-stilbene is formed in part during the preparation of the Grignard reagent and in part during the hydrolysis of the reaction mixture. Finally, bibenzyl is a normal side-product formed during the preparation of benzylmagnesium halides.

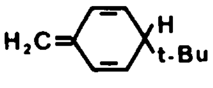
The "abnormal" products *o*- and *p*-t-butyltoluene might, *a priori*, be considered to be formed in three possible ways:

(i) Impurities in the magnesium used for the preparation of the benzylmagnesium halides could have initiated free-radical reactions.[7] However, the result of experiments in which very pure magnesium (DOW Chemical Corp., triply-sublimed; and Johnson, Matthey and Co. Ltd., Mg crystals) was used do not differ substantially from the result of an experiment in which 0·05 mole% anhydrous cobaltous chloride,[8] an initiator of free-radical Grignard reactions, was added to the reaction mixture. Thus it can be concluded that radicals are not involved.

(ii) The magnesium halide formed during the Grignard reaction and acting as a Friedel–Crafts catalyst[9] could have promoted the alkylation of toluene with t-butyl halides. To test this possibility a solution of toluene and t-butyl chloride was refluxed in the presence of anhydrous magnesium chloride. Neither in ether, nor in n-heptane, could any *o*- and *p*-t-butyltoluene be detected. It is also highly unlikely that ring-substituted products are formed in this way.

(iii) The third and most probable way of formation of the "abnormal" products is the attack of the partially negative *ortho* and *para* positions of the benzyl Grignard reagent on the t-butyl halide. Benkeser *et al.*[2a] suggested that in this kind of substitution triene intermediates exist in the reaction mixture before hydrolysis. In our case these intermediates can be formulated as:





These authors found that there was a large difference in the amount of ring-substituted toluenes present in samples, drawn from the same reaction mixture, hydrolysed either with saturated NH_4Cl or with mineral acid. We have been unable to observe the same effect. In the case of ether as a solvent the amount of "abnormal" products is too small to allow accurate measurements of any change. In n-heptane no difference could be detected between samples hydrolysed with saturated NH_4Cl or with 4N H_2SO_4. Furthermore, hydrolysis of samples drawn from another experiment in n-heptane with either D_2O or 10% D_2SO_4 in D_2O yielded *o*- and *p*-t-butyltoluene in which the amount of deuterium, determined by mass spectroscopy, was negligible. This indicates that, supposing the trienes are formed, their re-aromatization is complete before hydrolysis, at least in the case of n-heptane. Possibly the higher reaction temperature in this case is responsible for the difference between the observations made by Bankeser and our observations.

Next the influence of the solvent on the reaction course has been studied. A summary of the results is given in Table 1. Again the molar ratio was 1:1, except in experiments 6 and 7 in which t-butyl chloride acted not only as solvent, but also as reactant.

There is a striking difference between the results of the first five experiments and experiments 6–11. In the first experiments practically no ring-substituted toluenes

Table 1. Solvent influence on the reaction of benzylmagnesium chloride with t-BuCl

No.	Solvent	Mg used[c]	Yields %		
			NPB[b]	*o*tBT[b]	*p*tBT[b]
1	ether[a]	J & M	33·0	1·3	2·6
2	ether[a]	Fluka	46·1	1·8	1·8
3	ether[a]: benzene(2:1)	Fluka	45·1	0·5	0·5
4	THF[a]	Fluka	10·8	0·1	0·1
5	DME[a]	Fluka	18·6	0·2	0·2
6	t-BuCl	J & M	7·9	5·5	13·6
7	t-BuCl	Fluka	9·8	7·3	14·0
8	benzene	J & M	9·6	7·8	18·7
9	benzene	Fluka	13·4	7·4	21·2
10	n-heptane	J & M	7·1	6·8	12·9
11	n-heptane	Fluka	7·2	4·0	13·7

[a] Benzylmagnesium chloride was prepared in this solvent.

[b] NPB = neopentylbenzene, *o*tBT = *o*-t-butyltoluene, and *p*tBT = *p*-t-butyltoluene.

[c] Products from Johnson, Matthey & Co. Ltd. (Mg crystals), and Fluka AG (Mg für Grignardsynthesen) respectively.

were formed, but in the other six ring substitution prevailed over side-chain substitution. The explanation of this phenomenon has to be found in the solubility of the Grignard reagent. The first five experiments are homogeneous, the latter six heterogeneous, *i.e.* the benzyl Grignard reagent was insoluble. Our observations run parallel to those of Kornblum[10] and Curtin[11] in experiments on alkylation of phenoxide ions in different solvents. In homogeneous experiments O-alkylation takes place, in heterogeneous experiments ring alkylation dominates.

The low yield in experiment 4 is not unreasonable since any t-butylmagnesium chloride formed by the normally occurring exchange of functional groups[12] will react instantaneously with the solvent tetrahydrofuran.[13]

Finally the influence of substituents in the aromatic ring of the benzylmagnesium chloride has been investigated. The results of these experiments are collected in Table 2; again the molar ratio was 1:1.

For the time being it is hard to evaluate the influence on the relative rates of the two reactions: side-chain alkylation and ring alkylation. It would be expected that in the cases of the Me- and MeO-substituents both reactions will be accelerated as a result of the electron-donating character of the substituents. On the other hand the introduction of a bulky t-Bu group on a position *ortho* to a substituent will be hindered for steric reasons.[14] Finally, it is evident that in the cases of the 2- and 4-substituted benzylmagnesium chlorides one of the positions available for substitution is already occupied. In the cases of the 3-substituted Grignard reagents the position between the substituent and the CH_2MgCl-group will of course be very difficult to substitute.

Both substitution reactions will be slowed down in the cases of the Cl-substituted benzylmagnesium chlorides as a result of the electron-withdrawing character of the substituent; the steric factors are similar.

The results show that the steric factor played a prominent role. Even in the experiments conducted in n-heptane the amount of ring-substituted products is far less than

TABLE 2. SUBSTITUENT INFLUENCE ON THE REACTION OF BENZYLMAGNESIUM CHLORIDE WITH t-BuCl[a]

No.	R	Solvent	Yields %	
			$R\text{-}C_6H_4$-neoPent	$R\text{-}C_6H_3(Me)(t\text{-}Bu)$
12	2-Me	ether	51·0	—
13	2-Me	n-heptane	13·6	34·1[b]
14	3-Me	ether	55·0	—
15	3-Me	n-heptane	20·5	9·4
16	4-Me	ether	45·0	—
17	4-Me	n-heptane	27·1	11·9
18	3,5-diMe	ether	29·0	—
19	2-Cl	ether	40·0	—
20	3-Cl	ether	44·0	—
21	4-Cl	ether	26·0	—
22	3-MeO	ether	22·4	1·6[c]

[a] Fluka Mg used in all experiments.
[b] Two products: 3-t-Bu-*o*-xylene (6·8 %) and 4-t-Bu-*o*-xylene (27·3 %).
[c] One product: 2-t-Bu-5-Me-anisole.

the amount of "normal" product. 2-Methylbenzylmagnesium chloride being an exception, because here an unhindered position *para* to the CH_2MgCl-group is present.

Summarizing we can say that the formation of ring-substituted products in the reaction of benzylmagnesium halides with t-butyl halides is ascribed to the ambidency of the benzyl Grignard reagent. Neither the halide atoms present in both reactants nor the purity of the magnesium used for the preparation of the Grignard reagent influence the reaction course. On the other hand the solvent in which the reaction is conducted can play a very important role: if the experiment is heterogeneous, *i.e.* if the Grignard reagent is insoluble, the amount of ring-substitution prevails over side-chain substitution. In homogeneous experiments the reaction takes its "normal" course: only small amounts of ring-substituted products are formed. Finally, if the aromatic ring of the benzyl Grignard reagent is already substituted, steric factors restrict further ring substitution.

The reaction of t-butylmagnesium halides with benzyl halides, the inverse reaction, has until this moment hardly ever been used for the preparation of neopentyl-substituted aromatic compounds.[15] To find out if any ring-substituted products are formed in this reaction we treated some benzyl chlorides with a two-fold excess of t-butylmagnesium chloride in ether. An excess of Grignard reagent is necessary to convert all of the benzyl chloride. It has been reported[16] that unsubstituted benzyl chloride cannot be converted in this way: we can confirm this report. The results of these experiments are given in Table 3.

These data show that in this reaction three products are formed: the expected neopentylbenzene derivative, a reduction product and a dimerization product. No ring-substituted products have been detected. The two side-products are frequently encountered in this kind of condensation reaction.[17] We can confirm the observations of Kharasch and Reinmuth[18] that an alkyl substituent with its electron-donating

TABLE 3. REACTION OF 4-R-BENZYL CHLORIDES WITH t-BuMgCl

R	Yields %		
	$R-C_6H_4-CH_3$	$R-C_6H_4$-neoPent	$(R-C_6H_4-CH_2)_2$
H[a]	—[b]	10	20
Me	33	20	44
Et	26	21	44
i-Pr	40	19	39
t-Bu	31	19	42
neoPent	36	25	32

[a] 60% not converted.
[b] Not estimated.

character promotes the reaction by producing a more polar carbon-halide bond in the aralkyl halide.

Although the neopentylbenzene derivative is not contaminated with ring-substituted products, the relatively low yield makes this reaction not very attractive for the preparation of these compounds.

B. *Oxidation*

The three neopentyltoluenes have been oxidized to the corresponding neopentylbenzoic acids with alkaline $KMnO_4$ in aqueous pyridine. The general resistance of the neopentyl group has been reported previously,[19] although Blomquist and Westfahl[20] have found that the sodium salt of 4-neopentylbenzoic acid can be converted into the salt of 4-pivaloylbenzoic acid.

We can confirm both observations. Oxidation of 4-neopentyltoluene yielded, in addition to 4-neopentylbenzoic acid, 3% 4-pivaloylbenzoic acid. Neither *p*-toluic acid nor terephthalic acid could be detected in the crude mixture of acids isolated after the oxidation. The neutral fraction recovered from the oxidation mixture consisted of 10% 4-methylpivalophenone and 90% unconverted 4-neopentyltoluene. Similar observations were made in oxidation experiments with 2-neopentyltoluene.

The conclusion from these data is that the reactivity of the neopentyl group towards oxidation is much lower than that of the Me group. The explanation of this phenomenon can, in our view, be found in steric inhibition of resonance.[21] In the planar configuration of the benzyl-type radical formed during the first step of the oxidation of the neopentyl group there is an overlap of the Van der Waals radii of the *ortho* hydrogen atom of the aromatic ring and the Me groups of the t-Bu group.

The neopentyl group is thus not wholly indifferent towards oxidation, but once it is converted into the pivaloyl group further oxidation is prevented. This is probably due to the impossibility of enolization[22] caused by the absence of α-protons.

C. *Thermodynamic dissociation constants*

The pK_a^*-values of the neopentylbenzoic acids have been measured in 50 vol % EtOH. They are given in Table 4 together with the values of some other monoalkyl-substituted benzoic acids. From these values the σ_m- and σ_p-values have been calculated by means of the Hammett-equation. In 50 vol % EtOH the value of ρ is 1·525.[23] The σ-values are also given in Table 4.

TABLE 4. pK_a^*-VALUES OF SOME MONOALKYLBENZOIC ACIDS IN 50 VOL % EtOH DERIVED σ_m- AND σ_p-VALUES OF SOME ALKYL SUBSTITUENTS

R	pK_a^*			σ_m	σ_p
	2-R	3-R	4-R		
H	5·48	5·48	5·48	0·00	0·00
Me	5·51	5·60	5·70	−0·08	−0·14
Et	5·49	5·64	5·70	−0·10	−0·14
i-Pr	5·37	5·71	5·71	−0·15	−0·15
t-Bu	5·14	5·72	5·69	−0·16	−0·14
t-Pent	5·27	5·78	5·73	−0·20	−0·16
neoPent	5·67	5·78	5·72	−0·20	−0·16
n-Hept	—	—	5·71	—	−0·15
$CH_2Si(CH_3)_3$	—	5·81	5·85	−0·22	−0·24

The Table shows that the seven 4-alkylbenzoic acids have almost the same acidity in 50 vol % EtOH. They are all about 0·23 pK_a-units weaker than benzoic acid. Without going into more detail we can assume the absence of steric factors and an almost net electronic effect of the alkyl substituents.

The acidity of the 3-alkylbenzoic acids decreases with increasing bulkiness of the *meta* substituent. In the case of the two C_5-substituents, although of a different nature, primary and tertiary, the decrease is 0·30 pK_a-units. It is likely that we are dealing here with some steric hindrance of solvation of the carboxylate anion by bulky 3-alkyl substituents. It should be noted that we observed similar details as to acid-weakening effect in the 3-alkyl- and 3,5-dialkylcyclohexanecarboxylic acids.[24]

It is usual and not unreasonable to assume that the acidity of the 2-alkylbenzoic acids is determined by two opposing effects:[25] (i) steric inhibition of resonance resulting in an increased acidity and (ii) steric inhibition of solvation in the carboxylate anion, resulting in a decreased acidity.

Both effects become more prominent in going from Me to t-Bu as 2-alkyl substituent. As the acidity increases towards t-Bu substitution it is evident that the first effect dominates. The interesting observation that 2-neopentylbenzoic acid is definitely weaker than benzoic acid indicates that here the second effect, steric inhibition of solvation, is the more prominent one. A similar relative inhibition of solvation is found in 2-t-pentylbenzoic acid. This acid is weaker than 2-t-butylbenzoic acid.

An even larger acid-weakening effect has been found by Eaborn and Parker[26] in 2-(trimethylsilylmethyl)benzoic acid. They considered the large +I-effect of the substituent as the main cause. In view of our results it seems likely that the decrease of solvation due to steric factors is also of importance. The acid-weakening effect of the neopentyl group in 2-neopentylphenol should be noted for comparison.[27]

EXPERIMENTAL

A. *The Grignard reaction*

Standard procedure. In a dry 1 l. 5-necked flask, equipped with a stirrer, a thermometer, a condenser, and a dropping funnel both protected with drying tubes, and a gas-inlet tube, were placed 24·3 g Mg,* 50 ml

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* Quantitative analysis of the Mg used: DOW 10 ppm Mn, 17 ppm Fe, and 10 ppm Al; Johnson, Matthey 10 ppm Mn, 24 ppm Fe, and 24 ppm Al; Fluka 230 ppm Mn, 227 ppm Fe, 21 ppm Cu, 65 ppm Al, and 10 ppm Ni.

dry ether, and a crystal of I_2. 1·00 Mole freshly distilled benzyl halide in 400 ml dry ether was placed in the dropping funnel. In an atmosphere of dry N_2 about 10 ml ether soln was added; the reaction started almost at once. The rest of the soln was added over a period of 2 hr. After the addition was complete, the reaction mixture was refluxed for 30 min. The cooled soln of the benzylmagnesium halide was rapidly filtered into a dry 1 l. 5-necked flask. In case the experiment was to be conducted in another solvent, the ether was distilled off *in vacuo*, and 450 ml dry solvent added. 1·00 Mole t-butyl halide in 250 ml dry solvent was now slowly introduced. After all the t-butyl halide had been added the reaction mixture was refluxed for 18 hr. It was then cooled and 50 g Dry Ice added. When the excess had evaporated 125 ml satd NH_4Cl-soln was added with stirring, followed by 125 ml 4N H_2SO_4. The organic layer was separated off and the water layer was extracted with 2 × 125 ml portions ether. The combined organic layers were washed with water and extracted with 2 × 50 ml portions 2N KOH to remove phenylacetic acid. The organic layer was washed with water and dried over $MgSO_4$. The soln obtained was analysed by GLC, using n-decane or cumene as an internal standard. After the analysis the solvents were distilled off and the residue fractionated *in vacuo*.

Anhyd $MgCl_2$ as possible Friedel–Crafts catalyst. 0·25 Mole anhyd $MgCl_2$ (prepared according to Bryce-Smith[9] from $MgCl_2 \cdot NH_4Cl \cdot 6H_2O$), 0·25 mole toluene, and 0·25 mole t-BuCl in 175 ml dry solvent were refluxed for 18 hr. After cooling 30 ml satd NH_4Cl-soln followed by 30 ml 4N H_2SO_4 were added. The aqueous layer was separated off and extracted with 30 ml solvent. The combined solvent layers were washed with water, dried over $MgSO_4$ and analysed by GLC. In ether neither 2- nor 4-t-butyltoluene could be detected, in n-heptane less than 0·1% of 4-t-butyltoluene.

Experiments with deuterium exchange. A 100 ml sample drawn from a reaction conducted in n-heptane was hydrolyzed with 10 ml 99% D_2O. Another 100 ml sample was shaken with 10 ml 10% D_2SO_4 in D_2O. Both organic layers were dried over $MgSO_4$, and distilled over a spinning-band column. The fraction containing neopentylbenzene, and 2- and 4-t-butyltoluene was separated into the respective components by preparative GLC. All fractions were analyzed by MS. The amount of deuterium in the isolated products from both samples was negligible.

Neopentyltoluenes. These compounds were prepared in ether according to the standard procedure from the methylbenzyl chlorides. The starting materials were prepared from the corresponding xylenes and SO_2Cl_2 by the method of Kharasch and Brown.[28] The structures of the neopentyltoluenes were confirmed by PMR spectroscopy. The physical data of the hydrocarbons are given in Table 5. For the calibration of one GLC analysis *2-t-butyl-p-xylene* had to be synthesized: From 183·0 g 2-Br-*p*-xylene, 25·0 g Mg and 1 l. dry ether a soln of 2,5-diMe-phenylmagnesium bromide was prepared. To this soln was added 64·0 g dry acetone. The reaction mixture was kept overnight, cooled in an ice-bath and hydrolyzed with 200 ml satd NH_4Cl-soln. The layers were separated, the ether layer was washed 3 times with water, and dried. After evaporation of the ether *in vacuo* there remained 144·0 g crude *2-(2,5-dimethylphenyl)propan-2-ol*. The carbinol was taken up in 500 ml dry pet. ether (b.p. 60–80°) and cooled in an ice-salt bath. A rapid stream of HCl was bubbled through until no more water separated. The soln of *2-(2,5-dimethylphenyl)-2-chloropropane* was rapidly washed with 3 × 200 ml portions of ice-water, dried, and slowly added to a soln of 1·05 moles MeMgBr in 200 ml ether. The reaction mixture was refluxed for 5 hr and then hydrolyzed. After the customary work-up the 106·0 g residue was washed several times with conc. H_2SO_4, with water, and dried over $MgSO_4$. Distillation yielded 41·2 g (26%) pure 2-t-butyl-*p*-xylene, b.p. 92–93°/13 mm, n_D^{25} 1·5072 (lit[29] b.p. 213–217°/735 mm, $n_D^{28.5}$ 1·5003). (Found: C, 89·0; H, 11·1. Calc. for $C_{12}H_{18}$: C, 88·82; H, 11·18%). We also repeated the t-butylation of *p*-xylene according to Friedman:[30] the experiment yielded a very complex mixture of hydrocarbons. GLC analysis showed, however, that no 2-t-Bu-*p*-xylene had been formed.

TABLE 5. NEOPENTYLTOLUENES[36]

Compound	b.p.	n_D^{25}	Yield %	Calc. %		Found %	
				C	H	C	H
2-neoPent	79–80°/10 mm	1·4952	51	88·82	11·18	88·8	11·1
3-neoPent	203°/754 mm	1·4873	55	88·82	11·18	88·7	11·1
4-neoPent	84°/14 mm	1·4864	45	88·82	11·18	88·9	11·1

Separation of 2-t-Bu-p-xylene and 4-neopentyltoluene by thiourea inclusion. 21·0 g Mixture containing 93% 4-neopentyltoluene and 7% 2-t-Bu-*p*-xylene, resulting from an experiment in n-heptane, was added together with 25·0 g TU to 420 ml TU-soln in dry MeOH (200 g TU in 1250 ml MeOH). The inclusion compound, 57·0 g, was filtered off and treated with warm water. In the usual way there was obtained 8·1 g (41% recovery) 4-neopentyltoluene. The hydrocarbon mixture extracted from the filtrate was worked up and treated with a fresh portion of TU-soln. All fractions were combined and distilled to yield 15·9 g (81% recovery) pure 4-neopentyltoluene, b.p. 82–83°/13 mm, n_D^{25} 1·4866.

Substituted neopentylbenzenes. These compounds were prepared from the corresponding benzyl halides by the standard procedure. The relevant physical data are given in Table 6.

TABLE 6. SUBSTITUTED NEOPENTYLBENZENES

Compound	n_D^{25}	b.p.	Yield %	Calc. %		Found %	
				C	H	C	H
2-Cl	1·5082[a]	97–98°/15 mm	40	72·31	8·28	72·1	8·1
3-Cl	1·5033	93–94°/11 mm	44	72·31	8·28	72·2	8·1
4-Cl	1·5047[b]	101–102°/13 mm	26	72·31	8·28	72·2	8·2
3-MeO	1·4979	97–98°/ 9 mm	24	80·85	10·16	80·8	10·2
3,5-diMe	—[c]	87–89°/ 8 mm	29	88·57	11·43	88·7	11·3

[a] lit[31] n_D^{26} 1·5064.
[b] lit[31] n_D^{26} 1·5033.
[c] m.p. 36–37°.

Reaction of 4-alkylbenzyl chlorides with t-BuMgCl. To a soln of 1·00 mole of t-BuMgCl in 250 ml ether (prepared according to Kharasch and Reinmuth[32]) was added a soln of 0·5 mole 4-alkylbenzyl chloride in 150 ml ether. The reaction mixture was refluxed for 48 hr and then worked up in the usual way. The physical data of the 4-alkylneopentylbenzenes are given in Table 7.

TABLE 7. 4-ALKYLNEOPENTYLBENZENES

Compound	b.p.	n_D^{25}	Yield %	Calc. %		Found %	
				C	H	C	H
4-Et	108–109°/24 mm	1·4892	21	88·56	11·44	88·5	11·4
4-i-Pr	117–118°/22 mm	1·4898	19	88·35	11·65	88·4	11·5
4-t-Bu	128–129°/23 mm	1·4868	15	88·16	11·84	88·0	11·7
4-neoPent[b]	—[a]	—	25	88·00	12·00	88·0	12·1
2,4,6-triMe	122–124°/14 mm	1·5084	34	88·35	11·65	88·3	11·6

[a] m.p. 96·5–97·5°.

[b] The starting material *4-neopentylbenzyl chloride* was prepared as follows: To a mixture of 50·0 g neopentylbenzene and 45·0 g chloromethylmethylether in 135 ml dry CS_2 was added dropwise 27·0 g $SnCl_4$. The temp was kept below 0°. The mixture was stirred for 3 hr at this temp and then poured on ice. The organic layer was separated off, washed with ice-water and dried. The solvent was evaporated off and the residue distilled *in vacuo* to yield 42·8 g (66%) 4-neopentylbenzyl chloride, b.p. 132–134°/19 mm, n_D^{25} 1·5134. (Found: C, 73·4; H, 8·8; Cl, 18·1. Calc. for $C_{12}H_{17}Cl$: C, 73·26; H, 8·71; Cl, 18·03%). From the residue of the reaction of 4-neopentylbenzyl chloride with t-BuMgCl was isolated 10·9 g (32%) *4,4′-dineopentylbibenzyl*, m.p. 96–97°. (Found: C, 89·5; H, 10·6. Calc. for $C_{24}H_{34}$: C, 89·37; H, 10·63%).

B. *Oxidation*

Neopentylbenzoic acids. These acids were obtained from the corresponding neopentyltoluenes by oxidation with alkaline $KMnO_4$ in aqueous pyridine.[33] Samples from the crude mixture of acids were always treated with CH_2N_2 and analyzed by GLC. The neopentylbenzoic acids could easily be separated from the accompanying pivaloylbenzoic acids by recrystallization from aq. MeOH. Two of the acids were also prepared by the treatment of the Grignard reagent of the respective neopentylhalobenzenes with CO_2: 3-chloroneopentylbenzene yielded 44% 3-neopentylbenzoic acid and 4-bromoneopentylbenzene 50% 4-neopentylbenzoic acid. *4-Bromoneopentylbenzene* was prepared by the bromination of neopentylbenzene in the presence of Fe filings (86% yield), b.p. 111·5–112°/11 mm, n_D^{25} 1·5243 (lit[20] 62–63°/0·5 mm, n_D^{20} 1·5318; lit[31] n_D^{26} 1·5227). The neutral fraction obtained from the conversion of 4-bromoneopentylbenzene yielded *4,4'-dineopentylbiphenyl*, m.p. 141–141·5°. (Found: C, 89·7; H, 10·3. Calc. for $C_{22}H_{30}$: C, 89·73; H, 10·2%).

The structures of the neopentylbenzoic acids were confirmed by PMR spectroscopy. The physical data are summarized in Table 8.

TABLE 8. NEOPENTYLBENZOIC ACIDS

Compound	m.p.	Yield[a] %	Calc. %		Found %	
			C	H	C	H
2-neoPent	84·5–85·5°	31	74·97	8·39	75·0	8·4
3-neoPent	106–107°	52	74·97	8·39	74·9	8·3
4-neoPent	190·5–191°[b]	54	74·97	8·39	75·0	8·5

[a] Based on hydrocarbon converted.

[b] lit[20] 190·0–192·1°.

2-Neopentyltoluene was also oxidized with $KMnO_4$ in t-BuOH:H_2O (1:3). A mixture of acids was obtained in 40% yield consisting of 63% 2-neopentylbenzoic acid and 37% of an acid which could be identified by PMR spectroscopy and elemental analysis as *2-pivaloylbenzoic acid*, m.p. 118–119°. (Found: C, 70·0; H, 6·9. Calc. for $C_{12}H_{14}O_3$: C, 69·88; H, 6·84%).

For the identification of an unknown acid found in the oxidation product of 4-neopentyltoluene *4-pivaloylbenzoic acid* was prepared from 4-methylpivalophenone by the method of Nightingale and Janes.[34] It had m.p. 160·5–163°, Blomquist and Westfahl[20] reported for this acid, prepared by the oxidation of the Na-salt of 4-neopentylbenzoic acid, m.p. 158·9–161·6°.

C. *Thermodynamic dissociation constants*

The molar pK_a^*-values of the monoalkylbenzoic acids were calculated by means of an experimental determination of the proton activity of the buffered solns of the acids in 50 vol % EtOH. The Beckman pH-meter type G, with glass electrodes type G.P. and calomel electrode type 270, was set up for measurements with the N.P.S. phthalate buffer. The pH* of the buffered soln in 50 vol % EtOH is given by pH* = R − 0·15, in which R = the reading of the pH-meter. For further details see a recent publication from this laboratory.[35] We thank Mr. A. J. Hoefnagel for the measurements.

The preparation of all, except 4, monoalkylbenzoic acids has been described. The synthesis of 2- and 3-neopentylbenzoic acid has been given above, the synthesis of 2- and 3-t-pentylbenzoic acid is described here:

2-t-Pentylbenzoic acid. 288·0 g Me-*o*-toluate was added to a soln of 4·79 moles MeMgI in 1·7 l. dry ether. After 3 hr the reaction mixture was hydrolyzed and worked up in the usual way to yield 270·0 g (94%) crude *2-(2-methylphenyl)propan-2-ol*, which solidified upon standing. 265·0 g Carbinol was dissolved in 800 ml ether. During 5 hr a stream of dry HCl was bubbled through. Pentane was added and the organic layer was washed with ice-water and a 5% $NaHCO_3$aq. After drying over $MgSO_4$ the soln of crude *2-(2-methylphenyl)-2-chloropropane* was added to a soln of 4·6 moles EtMgBr in 2 l. ether. The reaction mixture was kept overnight and then refluxed for 1 hr. After the customary work-up the residue remaining after evaporation of the solvents was shaken with 100 ml portions of conc H_2SO_4, washed with water, and dried. Distillation *in vacuo* yielded 93·0 g (32%) *2-t-pentyltoluene*, b.p. 98–100°/18 mm, n_D^{25} 1·5076. (Found: C, 88·8; H, 11·1. Calc. for $C_{12}H_{18}$: C, 88·82; H, 11·18%). 47·5 g Hydrocarbon was oxidized[33] to yield 15·2 g (30%) *2-t-pentylbenzoic acid*, m.p. 84·5–85·5°. (Found: C, 75·1; H, 8·4. Calc. for $C_{12}H_{16}O_2$: C, 74·97; H, 8·39%). 9·0 g (18%) 2-t-Pentyltoluene was recovered from the neutral fraction, b.p. 116–117°/31 mm.

3-t-Pentylbenzoic acid. 102·0 g Me-*m*-toluate yielded 72·5 g (71 %) *2-(3-methylphenyl)propan-2-ol*, b.p. 70–71°/0·8 mm, n_D^{25} 1·4959. 100·0 g Carbinol was converted into 105·2 g crude *2-(3-methylphenyl)-2-chloropropane*. 15·0 g Carbinyl chloride yielded 2·20 g (15 %) *3-t-pentyltoluene*, b.p. 92–93°/16 mm, n_D^{25} 1·4959, purity 98 % according to GLC analysis. (Found: C, 88·8; H, 11·1. Calc. for $C_{12}N_{18}$: C, 88·82; H, 11·18 %). 2·17 g Hydrocarbon was oxidized[33] to yield 1·29 g (50 %) *3-t-pentylbenzoic acid*, m.p. 75–75·5°. (Found: C, 74·9; H, 8·4. Calc. for $C_{12}H_{16}O_2$: C, 74·97; H, 8·39%).

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[36] *Note added in proof*: Dr. Walton informed us that the refractive indices of the neopentyltoluenes reported [A. R. Bassindale, C. Eaborn and D. R. M. Walton, *J. Chem. Soc.* C, 2505 (1969)] are in error. They redetermined the refractive index of *p*-neopentyltoluene as n_D^{25} 1·4858, which is in agreement with our value. The PMR results for the three isomers agreed with our figures to within experimental error.